

シクロプロペンの開環を鍵とした新規タンデム  
反応の開発

Development of Novel Tandem Reactions via  
Ring-Opening of Cyclopropenes

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The tandem allylation reaction via ring-opening of cyclopropenes was achieved. The present reaction involves the generation of carbenoid intermediates from cyclopropenes *in situ*, which give multifunctionalized allylmetal intermediates via trapping reaction with organometallic reagents. The present reaction could afford the various allylated products in a single operation. Furthermore, the related reactions of the cyclopropenes were also developed.

## Abstract

### Development of Novel Tandem Reactions via Ring-Opening of Cyclopropenes

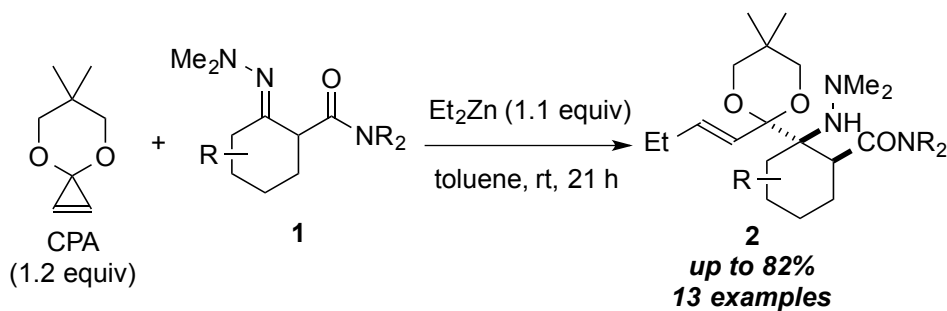
Takeo Nakano

C–C bond activation is the powerful approach to the design of novel selective and efficient synthesis of structurally complex molecules in single operation. Therefore, many groups have developed the methods of C–C bond activation using metal complexes. However, in previous reports, the expensive transition metal catalyst or high temperature was required to realize the activation of C–C bond. Furthermore, the selectivity of C–C bond cleavage is difficult to control. From these view, the development of the more efficient method of C–C bond activation is a challenging task.

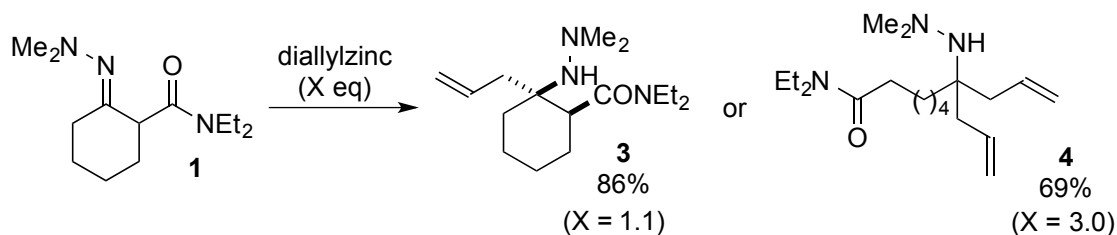
In the present paper, the tandem allylation reaction via ring-opening of cyclopropenes was reported. The present reaction includes the generation of multi-functionalized allylmetal intermediate to give the various homoallylic alcohol derivatives, which are widely used for synthetic intermediates toward natural products.

## Chapter 1

The tandem allylation reaction using allylzinc intermediates from cyclopropenes was achieved. The cyclopropenone acetal (CPA) was used as a substrate for the generation of vinylcarbene intermediates due to the stabilization by the coordination of an acetal moiety on a Zn center. Furthermore, the allylzinc intermediate from CPA acts as a novel acylanion equivalent to add the cyclic  $\beta$ -hydrazoneamide **1**. The present reaction gave the sterically congested hydrazine products **2** as a single diastereomer.

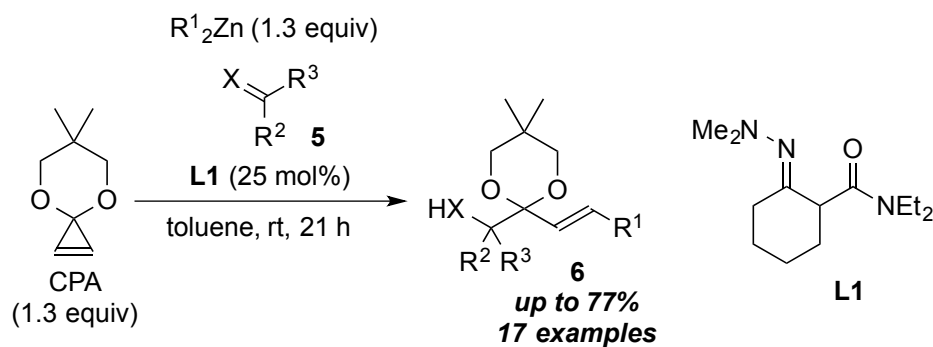


In chapter 1, the allylation reaction of  $\beta$ -hydrazoneamides **1** with diallylzinc was also reported. The diallylzinc was activated by coordinative substrates to add the unactivated carbonyl derivatives smoothly. When an excess amount of diallylzinc was used, the diallylation of hydrazone proceeded via cleavage of amide moiety like a retro-Manich reaction.



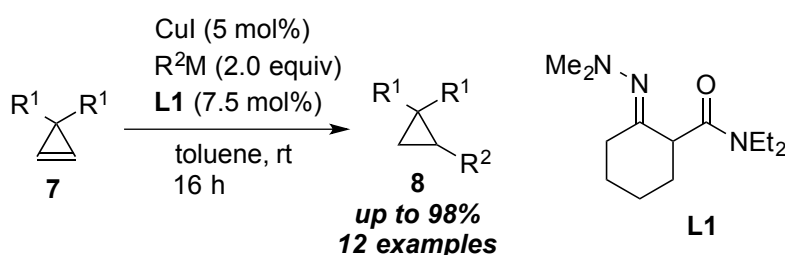
## Chapter 2

The allylzinc intermediate allowed the addition to the external electrophiles **5**; aldehydes, an aldimine and a ketone. In the present reaction, the  $\beta$ -hydrazoneamide **L1** acts as a ligand to promote the generation of allylzinc intermediate. As a result, a wide variety of functionalized homoallylic alcohols or amine were obtained in a one-pot procedure.

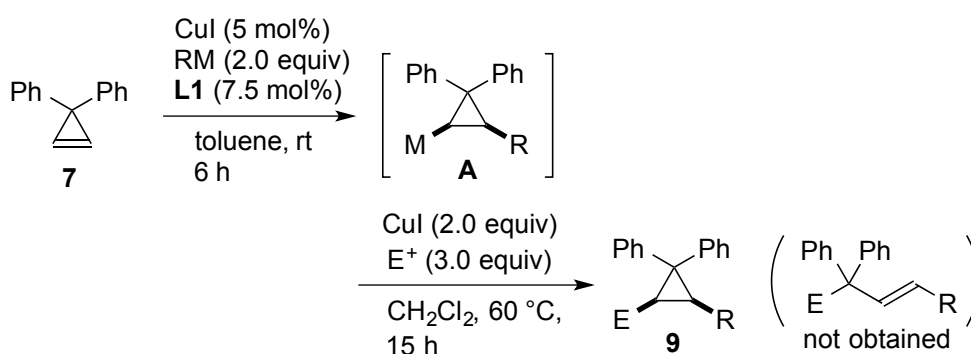


### Chapter 3

The Cu-catalyzed carbometallation of unfunctionalized cyclopropenes **7** was described. Chapter 1 and 2 describes the tandem allylation reaction proceeded via carbene intermediate as a working hypothesis. However, there is another possibility; the initial step of the allylation reaction was carbozincation of cyclopropenes. Therefore, the generation of cyclopropylzinc intermediates was examined via carbozincation of various cyclopropenes for the subsequent ring-opening to give allylzinc intermediates. As a result, the various cyclopropane products were obtained in high yields.

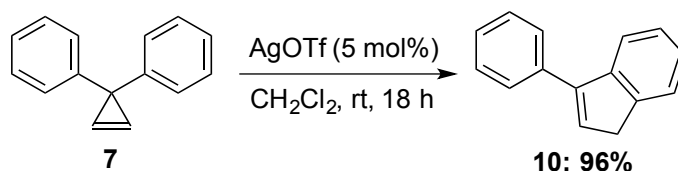


Furthermore, the electrophilic trapping of the cyclopropylzinc intermediate **A** was demonstrated. The trapping reaction gave the multifunctionalized cyclopropanes, however, the allylation reaction via ring-opening of cyclopropylzinc did not occur. The present result suggests that the ring-opening of cyclopropene might not proceed via the carbozincation of cyclopropenes to generate cyclopropylzinc intermediates.

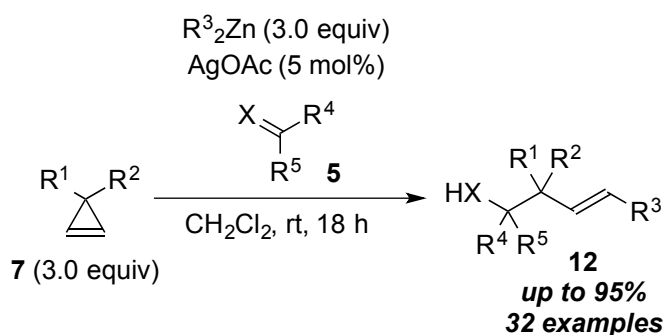


## Chapter 4

Silver-catalyzed ring-opening of cyclopropenes via carbene intermediates was achieved. As a result of screening of metal catalyst, AgOTf gave the indene product **10** in high yield via vinylcarbenoid from cyclopropene **7**.



The generation of allylmetal intermediate by the trapping reaction of silver carbene intermediate using organometallic reagent was investigated. In the present reaction, the use of dialkylzinc reagent and AgOAc allowed the multifunctionalized allylzinc intermediates from cyclopropenes **7**. The various homoallylic alcohol derivatives were obtained via allylation reaction of carbonyl derivatives **5**.





## 学位論文審査報告書（甲）

1. 学位論文題目（外国語の場合は和訳を付けること。）

Development of Novel Tandem Reactions via Ring-Opening of Cyclopropenes

（シクロプロペンの開環を鍵とした新規タンデム反応の開発）

2. 論文提出者 (1) 所 属 物質科学専攻

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中野 健央

3. 審査結果の要旨（600～650字）

提出学位論文について、審査委員によって審査をした後、各審査委員により個別に予備審査を実施するとともに、平成27年2月3日に開催された口頭発表の結果を踏まえて、同日に論文審査委員会を開催して協議を行った。その結果、以下の様に判定した。

高価な遷移金属を用いず、簡便な手法により、穏和な条件下での連続的炭素炭素結合切断／形成反応の開発は、グリーンケミストリーの面からも重要な課題である。本論文では、特異な反応性を有する歪んだシクロプロペンに着目し、連続的炭素-炭素結合切断／形成反応について検討した結果について述べたものである。すなわち、各種シクロプロペンに各種金属試薬を作用させるとメタルカルベノイドが生成することを見出し、有機金属試薬への挿入が進行することを初めて明らかにした。さらに生成するアリルアニオンの求電子的捕捉により、高度に官能基化されたヒドラジン型生成物が一挙に得られることを明らかにした他、アルデヒド等の外部求電子剤での捕捉にも成功して官能基化されたホモアリルアルコール合成へ展開するなど、高度に官能基化された各種化合物の合成を数多く実現した。本論文の内容は、多様な連続的反応の開発や生理活性化合物合成への発展性を秘めており、有機合成化学的に非常に意義深いことから、博士（理学）の学位に値するものと判断した。

4. 審査結果 (1) 判 定（いずれかに○印） 合 格 ・ 不合格

(2) 授与学位 博士（理学）